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EXAMINER	
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1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/981,020	Applicant(s) KOHANE ET AL.	
	Examiner Liliana Di Nola-Baron	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-65 and 80-85* is/are pending in the application.

4a) Of the above claim(s) *21,22,26,29,31-36 and 38-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-20,23-25,27,28,30,37,46-65 and 80-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

4. Claims 63 and 64 are rejected under 35 U.S.C. 102(b) as being anticipated by Moynihan (U.S. Patent 5,589,189).

Moynihan discloses a process for forming liposome-encapsulated hemoglobin and teaches that the compositions are formed by adding to a neutral lipid, such as dipalmitoylphosphatidylcholine (DPPC), hemoglobin dispersed in sucrose or lactose solution and human serum albumin, and filtering the resulting compositions to produce particles having a median size of 0.09-0.15 microns (See col. 5, lines 1-58). Liposomes, classified in class 424/ 450, are microparticles, thus, the patent teaches microparticle compositions comprising an active agent (hemoglobin) encapsulated in a matrix comprising a lipid (DPPC), a protein (human serum albumin) and a sugar (lactose).

Regarding the method of administering the particles claimed in claims 63 and 64 of the application, Moynihan teaches that the liposome fluid of the invention can be administered to patients as a blood substitute by transfusion (See col. 1, lines 8-12) and the aqueous dispersions of liposomes can be delivered intravenously (See col. 2, line 67 to col. 3, line 2), thus the patent contemplates injection of the liposome composition into a patient.

The administration of liposome compositions to a patient provided by Moynihan meets the limitations of claims 63 and 64 of the instant application, as the patent contemplates compositions comprising an agent encapsulated in a matrix comprising lipid, protein and sugar,

DETAILED ACTION

Receipt of Applicant's amendment and declaration, filed on August 25, 2003, is acknowledged.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 2, 6-20, 23-25, 27, 28, 30, 37, 46-61 and 80-85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment to claims 1, 2, 6-20, 23-25, 27, 28, 30, 37, 46-61 and 80-85, changing the claim language to solid microparticles represents a departure from the specification and the claims as originally filed and Applicant has not pointed where the support for said amendment comes from.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

and a method of administering the microparticles to a patient. Thus, Moynihan anticipates the claimed invention.

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 1, 2, 6, 7, 13, 17-20, 23-25, 27, 28, 30, 37, 46, 48-53, 57-60, 62-65 and 80-85 are rejected under 35 U.S.C. 102(a) as being anticipated by Bot et al. (WO 00/00215).

Bot et al. provides solid microparticle compositions (See p. 25, lines 14-15 and p. 26, line 5). With regard to claims 1, 2, 6, 30, 37, 46, and 81-83, Bot et al. teaches that the bioactive agent is encapsulated in a matrix (See p. 9, line 11 to p. 10, line 16), and the matrix comprises a phospholipid (See p. 21, lines 25-27), synthetic or natural polymers or combinations thereof, including albumin, and disaccharides, such as lactose (See p. 24, lines 3-25). Thus, Bot et al. discloses pharmaceutical compositions comprising an agent encapsulated in a matrix comprising lipid, protein, sugar and synthetic polymer, as claimed in instant claims 2 and 81, or just lipid, protein (albumin) and sugar (lactose), as claimed in claims 1, 30, 37 and 46, or protein and sugar, as claimed in claim 6, or protein and synthetic polymer, as claimed in claim 82, or sugar and synthetic polymer, as claimed in claim 83.

With regard to claims 7, 13 and 20, the agent disclosed by Bot et al. is a therapeutic protein and can be a vaccine, which is a prophylactic agent (See p. 9, lines 11-28).

With respect to claims 18-20, 23-25, 27 and 28, the dipalmitoylphosphatidylcholine disclosed by the prior art (See p. 21, lines 25-27 and p. 22, lines 18-29) is a naturally occurring phosphatidylcholine with no charge, an emulsifier and a surfactant, as claimed in claims 18-20, 23-25, 27 and 28 of the instant application.

Regarding claims 48-50, Bot et al. teaches that the microparticles may comprise up to 100% of a surfactant, such as a phospholipid (See p. 23, lines 18-26).

With regard to claims 51-53, Bot et al. teaches that the microparticles may comprise up to 100% of bioactive agent (protein), and the protein can be in the matrix (See p. 9, line 29 to p. 10, line 12).

With respect to claims 57-60 and 80, Bot et al. provides particles having a size of 0.5-50 microns (See p. 26, lines 11-23).

With regard to claims 62, 84 and 85, Bot et al. teaches that the microparticles of the invention are formed by spray drying (See p. 32, line 26 to p. 33, line 14).

Regarding claims 63-65, Bot et al. teaches that the preparations may be administered by injection (See p. 41, lines 2-5) and are delivered into body cavities (See p. 40, lines 23-27).

The compositions disclosed by Bot et al. meet the limitations of claims 1, 2, 6, 7, 13, 17-20, 23-25, 27, 28, 30, 37, 46, 48-53, 57-60 and 80-85, as the international publication contemplates pharmaceutical compositions comprising an active agent encapsulated in a matrix comprising lipid, protein, sugar and synthetic polymer, and methods of preparing and administering said compositions. Thus, Bot et al. anticipates the claimed invention.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 2, 6, 7, 13, 16, 18-20, 23-25, 27, 28, 30, 37, 46 and 57-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moynihan (U.S. Patent 5,589,189).

Moynihan discloses a process for forming liposome-encapsulated hemoglobin and teaches that the compositions are formed by adding to a neutral lipid, such as dipalmitoylphosphatidylcholine (DPPC), hemoglobin dispersed in sucrose or lactose solution and human serum albumin, and filtering the resulting compositions to produce particles having a median size of 0.09-0.15 microns (See col. 5, lines 1-58). Liposomes, classified in class 424/ 450, are microparticles. Moynihan does not specifically teach that the liposome formulations are solid, however, the patent teaches that the liposome formulation is suitable for lyophilization (See col. 4, lines 50-

51). Lyophilization produces solid, dry particles. Thus, it would have been obvious to one of ordinary skill in the art to apply the teachings of the patent to device microparticle compositions comprising an active agent (hemoglobin) encapsulated in a matrix comprising a lipid (DPPC), a protein (human serum albumin) and a sugar (lactose), as claimed in claims 1 and 2 of the instant application, or an agent encapsulated in a matrix comprising protein and sugar, as claimed in instant claim 6.

With respect to the subject matter claimed in claims 7, 13 and 16 of the application, the process claimed in claim 1 of the patent comprises forming a liposome dispersion containing a therapeutic or an imaging (diagnostic) agent, and the hemoglobin disclosed by the patent (See col. 5, lines 26-28) is a protein.

The dipalmitoylphosphatidylcholine disclosed by the prior art is a naturally occurring phosphatidylcholine with no charge, an emulsifier and a surfactant, as claimed in claims 18-20, 23-25, 27 and 28 of the instant application.

Moynihan provides particles comprising human serum albumin and lactose (See col. 5, lines 34-42), as claimed in claims 30, 37 and 46 of the instant application.

With respect to the size of the microparticles claimed in claims 57-61 of the application, Moynihan teaches that the liposomes of the invention have a median size of 0.09 to 0.15 microns.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of Moynihan to device pharmaceutical compositions comprising solid microparticles of an agent encapsulated in a matrix. The expected result would have been a successful pharmaceutical composition. Because of the teachings of Moynihan, that liposome formulations may be lyophilized and used to deliver active agents, one of ordinary skill in the art would have a reasonable expectation that compositions of solid microparticles would be successful in delivering active agents. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

8. Claims 1, 2, 6, 7, 12-20, 23-25, 27, 28, 30, 37, 46-65and 80-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernstein et al. (U.S. Patent 6,423,345).

Bernstein et al. discloses polymer matrices in the form of microparticles, wherein a lipid, preferably dipalmitoylphosphatidylcholine (DPPC), is integrated into the polymeric matrix (See col. 1, lines 10-66, col. 2, lines 15-48 and col. 5, lines 1-65).

With respect to the matrix components claimed in claims 1, 2, 6, 81-83 and 85, Bernstein et al. teaches that the matrix can be formed of synthetic or natural polymers, including proteins, such as albumin, and polysaccharides (sugars) (See col. 3, line 31 to col. 4, line 22), thus the patent contemplates a matrix made of synthetic polymer, lipid, protein, or sugar. Bernstein et al. does not specifically teach a matrix comprising all four of said components, however, the patent

provides the general teachings that synthetic polymer, lipid, protein and sugar can all be used to form the matrix of solid microparticles.

With regard to the limitation, that the agent is encapsulated in a matrix, Bernstein et al. includes therapeutic and prophylactic agents among the active agents, which can be incorporated into the matrix (See col. 6, line 56 to col. 7, line 5).

The dipalmitoylphosphatidylcholine disclosed by Bernstein et al. is an emulsifier and a surfactant, thus the patent contemplates a matrix made of a lipid and protein, and specifically albumin and dipalmitoylphosphatidylcholine, which are matrix components claimed in claims 1, 2, 6, 18-20, 23-25, 27, 28, 30, 81 and 85 of the instant application.

With respect to the presence of the sugar in the matrix claimed in claims 1, 2, 6, 7, 12-20, 23-25, 27, 28, 30, 37, 46-60, 62-65, 81, 83 and 85 of the instant application, Bernstein et al. provides the general teachings that sugars can be included in the matrix (See col. 4, lines 19-22), and the microparticles can be combined with bulking agents, including sugars, such as lactose (See col. 10, lines 6-10).

Bernstein et al. contemplates pharmaceutical compositions comprising the microparticles of the invention, as it teaches that the microparticles of the invention can be administered as a powder, or formulated in tablets or capsules, or suspended in a solution with pharmaceutically acceptable carriers (See col. 9, lines 35-47).

With regard to the agents claimed in claims 7 and 12-17 of the application, Bernstein et al. teaches that therapeutic and prophylactic agents can be incorporated into the matrix and includes proteins, sugars, steroids (lipids) and vasodilators among the drugs delivered by the invention (See col. 6, line 56 to col. 7, line 5). The agents described by Bernstein et al. as those that may be labeled with a fluorescent label or an enzymatic or chromatographically detectable agents (See col. 6, lines 61-63) are diagnostic agents.

With respect to the amounts of lipid, protein and sugar claimed in claims 48-56 of the instant application, Bernstein et al. teaches that the content of the lipid in the matrix is 0.01-60% in relation to the content of the polymer (See col. 6, lines 18-21) and the amount of polymer (protein) is 0.1-60% (See col. 4, lines 62-64). Thus, the patent contemplates an amount of lipid up to 36%.

With respect to the size of the microparticles claimed in claims 57-60 and 80 of the application, Bernstein et al. teaches that the microparticles of the invention are manufactured with a diameter suitable for the intended route of administration, and discloses particles for intravascular administration having a diameter of 0.5 to 8 microns (See col. 2, lines 20-27).

With regard to the particle size claimed in instant claim 61, Bernstein et al. is deficient in the sense that the patent fails to disclose particles smaller than 0.5 microns. Applicant has not established the criticality of the small size of particles claimed in the instant application and there is no comparable example in the specification to demonstrate that the claimed small size

provides some unusual and/or unexpected results. It appears to the examiner that the smaller size of particles does nothing additional to the compositions of the invention, especially in view of the teachings of the prior art, that the microparticles of the invention can be administered by any route, including administration to the lungs (See col. 9, lines 56-63).

With respect to the method of preparing the microparticles claimed in claims 62, 84 and 85, Bernstein et al. teaches that the microparticles of the invention can be produced by spray drying by dissolving the polymer (protein) and the lipid in the appropriate solvent, dispersing the active agent into the polymer solution, and then spray drying the polymer solution to form microparticles (See col. 8, lines 18-33).

With regard to the method of administering an agent claimed in claims 63-65 of the application, Bernstein et al. teaches that the microparticles are combined with a pharmaceutically acceptable carrier and administered to a patient by injection into a blood vessel, subcutaneously, intramuscularly or orally (See col. 9, line 64 to col. 10, line 6). Oral administration implies placing the microparticles in the oral cavity of the patient, thus the patent contemplates placing the microparticles in a body cavity of the patient, as claimed in claim 65 of the instant application.

With respect to the ratio of lipid to protein to sugar claimed in claim 47 of the application, Applicant has not established the criticality of the high ratio of lipid claimed in the instant application and there is no comparable example in the specification to demonstrate that the

claimed high ratio of lipid provides some unusual and/or unexpected results. It appears to the examiner that the higher ratio of lipid does nothing additional to the compositions of the invention, especially in view of the teachings of the prior art, that the hydrophobic compound integrated in the polymeric matrix modifies the diffusion of water into the microparticle and the diffusion of solubilized drug out of the matrix (See col. 2, lines 8-11).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of Bernstein et al. to devise microparticles for the controlled delivery of drugs. The expected result would have been a successful microparticle composition, and successful methods of preparing said composition and administering said composition to a patient. Because of the teachings of Bernstein et al., that microparticles comprising synthetic polymer, protein, lipid and/or sugar can be used for drug delivery, one of ordinary skill in the art would have a reasonable expectation that the compositions and methods claimed in the instant application would be successful in delivering an active agent to a patient. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

9. Claims 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernstein et al., as applied to claims 1, 2, 6, 7, 12-20, 23-25, 27, 28, 30, 37, 46-60, 62-65 and 80-85 above, and further in view of Goldenheim et al. (U.S. Patent 6,534,081).

The teachings of Bernstein et al. have been summarized above. The prior art is deficient in the fact, that it does not specifically include the anesthetics recited in claims 8-10 of the application and anticonvulsant agents, as claimed in claim 11, among the therapeutic agents encapsulated in the microparticles of the invention.

Goldenheim et al. provides sustained release dosage forms comprising a local anesthetic and an augmenting agent, and includes bupivacaine, dibucaine, tetracaine and lidocaine among the preferred local anesthetics used in the invention (See col. 3, line 50 to col. 4, line 51). Goldenheim et al. teaches that the local anesthetic is prepared in matrices of controlled release injectable microspheres (See col. 5, lines 60-64), and the formulations of the invention are suitable for administration in all body spaces and cavities (See col. 6, lines 55-59). Goldenheim et al. discloses formulations comprising microparticles comprising a local anesthetic, an augmenting agent and a sustained release polymer selected from synthetic polymers, proteins, polysaccharides and combinations thereof (See col. 7, lines 20-47). Thus, the patent provides the general teachings that local anesthetics can be delivered by microparticle compositions and specifically discloses the compounds recited in claims 8-10 of the instant application.

With respect to claim 11, Goldenheim et al. includes anticonvulsants among the augmenting agents incorporated in the compositions of the invention (See col. 12, lines 9-12).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to combine the teachings of Bernstein et al. with the teachings of

Goldenheim et al., to obtain microparticles for the controlled delivery of local anesthetics and anticonvulsant drugs. The expected result would have been successful microparticle compositions for the delivery of local anesthetics and drugs. Because of the teachings of Bernstein et al., that microparticle formulations comprising an agent encapsulated in a matrix comprising lipid, protein and sugar are suitable for the administration of drugs, and the teachings of Goldenheim et al., that local anesthetics and anticonvulsants may be delivered using microparticle formulations, one of ordinary skill in the art would have a reasonable expectation that the compositions claimed in the instant application would be successful in delivering an active agent to a patient. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

10. Claims 47, 54-56 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bot et al. (WO 00/00215).

The teachings of Bot et al. have been summarized above. With regard to claims 47 and 54-56, Bot et al. is deficient in the sense, that the prior art does not specifically disclose the ratio of lipid to protein to sugar and the amount of sugar in the matrix. It is the view of the examiner that the skilled artisan would have been able to determine the optimal ratio between the matrix components and amount of sugar by routine experimentation. With regard to claim 61, Bot et al. fails to disclose particles smaller than 0.5 microns. Applicant has not established the criticality of the small size of particles claimed in the instant application and there is no comparable example in the specification to demonstrate that the claimed small size provides some unusual and/or

unexpected results. It appears to the examiner that the smaller size of particles does nothing additional to the compositions of the invention, especially in view of the teachings of the prior art, that the microparticles of the invention can be administered by any route, including inhalation (See p. 41, lines 6-34).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to determine the optimal ratio of lipid to protein to sugar and optimal amount of sugar in the matrix of the microparticles disclosed by Bot et al. by routine experimentation to obtain pharmaceutical compositions having the desired release rate of the active agent encapsulated in the matrix. The expected result would have been a successful drug delivery composition. Because of the teachings of Bot et al., that microparticles containing lipid, protein and sugar may be used to deliver active agents, one of ordinary skill in the art would have a reasonable expectation that the compositions claimed in the instant application would be successful in delivering active agents. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

11. Claims 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bot et al. (WO 00/00215) in view of Goldenheim et al. (U.S. Patent 6,534,081).

The teachings of Bot et al. have been summarized above. The prior art is deficient in the fact, that it does not specifically include the anesthetics recited in claims 8-10 of the application and anticonvulsant agents, as claimed in claim 11, among the therapeutic agents encapsulated in the

microparticles of the invention, and it does not teach microparticles having a diameter of less than 500 nanometers, as claimed in claim 61 of the instant application.

Goldenheim et al. provides sustained release dosage forms comprising a local anesthetic and an augmenting agent, and includes bupivacaine, dibucaine, tetracaine and lidocaine among the preferred local anesthetics used in the invention (See col. 3, line 50 to col. 4, line 51). Goldenheim et al. teaches that the local anesthetic is prepared in matrices of controlled release injectable microspheres (See col. 5, lines 60-64), and the formulations of the invention are suitable for administration in all body spaces and cavities (See col. 6, lines 55-59). Goldenheim et al. discloses formulations comprising microparticles comprising a local anesthetic, an augmenting agent and a sustained release polymer selected from synthetic polymers, proteins, polysaccharides and combinations thereof (See col. 7, lines 20-47). Thus, the patent provides the general teachings that local anesthetics can be delivered by microparticle compositions and specifically discloses the compounds recited in claims 8-10 of the instant application.

With respect to claim 11, Goldenheim et al. includes anticonvulsants among the augmenting agents incorporated in the compositions of the invention (See col. 12, lines 9-12).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to combine the teachings of Bot et al. with the teachings of Goldenheim et al., to obtain microparticles for the controlled delivery of local anesthetics and anticonvulsant drugs. The expected result would have been successful microparticle compositions for the

delivery of local anesthetics and drugs. Because of the teachings of Bot et al., that microparticle formulations comprising an agent encapsulated in a matrix comprising lipid, protein and sugar are suitable for the administration of drugs, and the teachings of Goldenheim et al., that local anesthetics and anticonvulsants may be delivered using microparticle formulations, one of ordinary skill in the art would have a reasonable expectation that the compositions claimed in the instant application would be successful in delivering an active agent to a patient. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

12. Applicant's arguments filed on August 25, 2003 have been considered but are moot in view of the new ground(s) of rejection.

13. Applicant's amendment has overcome the 35 U.S.C. 112, second paragraph rejection of claim 28 of the previous Office action. Accordingly, said rejection is withdrawn.

14. The 35 U.S.C. 102(e) rejection of claims 1-7, 13, 18-20, 23-25, 27, 28, 30 37, 46-59 and 62-64 over Edwards et al. (U.S. Patent 5,985,309) of the previous office action is withdrawn in view of Applicant's declaration, stating that the subject matter claimed in U.S. Patent 5,985,309 was not invented by another.

Conclusion

15. Claims 1, 2, 6-20, 23-25, 27, 28, 30, 37, 46-65 and 80-85 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318 (571-272-0592 after February 3, 2004). The examiner can normally be reached on Monday through Thursday, 8:30AM-7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927 (571-272-0602 after February 3, 2004). The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

LDNB3

January 28, 2004

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600